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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/546,201	POLO ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28-31 and 33-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28-31 and 33-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

The request received on June 1, 2004 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/546,201 is acceptable and a RCE has been established. An action on the RCE follows. Claims 26, 28-31 and 33-44 are pending and under consideration.

Drawings

Applicant requests confirmation regarding the replacement Figure 6 mailed November 26, 2003.

The replacement sheet for Figure 6 was received on November 28, 2003. This drawing is acceptable.

Sequence Listing

Applicant also requests confirmation that the sequence listing mailed November 26, 2003 was received and that the amendments to the specification were made.

This sequence listing was also received November 28, 2003 and amendments to the specification were made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26, 28-31 and 33-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky, Jr. et al. (US 6,015,686), which is hereinafter referred to as

"Dubensky", Cella et al. (Journal of Experimental Medicine. March 1, 1999; 189 (5): 821-829), hereinafter "Cella", Chada et al. (US 5,736,388), hereinafter "Chada" and Gillespie et al. (WO 90/14090), hereinafter "Gillespie".

Claim 26 to require that the double stranded RNA (dsRNA) has self-complementing sequences within the RNA.

Claim 26 has been amended to encompass an expression cassette comprising:

1) a promoter operably linked to a nucleic acid molecule, which when transcribed *in vivo*, forms double stranded RNA via self-complementing sequences, that induces the production of interferon and

2) RNA polymerase II operably linked to a nucleic acid encoding an antigen from a pathogenic agent.

Claims 28 and 29 state that the antigen is a viral antigen selected from HIV, HSV, HBV, HCV, HPV and FIV. Claim 30 states that the pathogenic agent is a bacteria, a parasite or a fungus and claim 31 states that the pathogenic agent is a tumor. Claim 33 requires that the pol II promoter is selected from CMV, SV40, MoMLV LTR and RSV LTR. Claim 34 is drawn to a gene delivery vector comprising the instant expression cassette. Claim 44 is drawn to a cell containing the gene delivery vector of claim 34. Claims 35-43 state that the vector is a plasmid, a recombinant retrovirus, a recombinant herpesvirus, a recombinant poxvirus, a recombinant adenovirus, a recombinant parvovirus, a recombinant alphavirus, a recombinant polyomavirus, and a eukaryotic layered vector initiation system, respectively.

Dubensky teaches a eukaryotic layered vector initiation system comprising a promoter that expresses a heterologous sequence, see claims 1 and 2. The heterologous

sequence is derived from a virus and is selected from HIV, HBV, HCV, FIV, see claim 9, as well as HSV and HPV, see column 4, lines 36-39. Dubensky also teaches that the vector construct can encode proteins from bacteria, parasites or fungus, see column 23, lines 30-36. Additionally, the vector of Dubensky encodes a cancer gene, see column 27, line 60 to column 28, line 2.

The promoter that initiates the synthesis of viral RNA encoding the heterologous gene of Dubensky is selected from the group consisting of the following: CMV, SV40, MoMLV LTR and RSV LTR, see claim 7, column 12, lines 54-62, column 55, lines 14-34, column 100, lines 55-56, column 101, lines 42-57. These promoters are identical to the promoters listed in instant claim 33.

Dubensky teaches that a wide variety of vectors may be utilized in the eukaryotic layered vector initiation system, such as retroviruses, herpesviruses, poxviruses, adenoviruses, parvoviruses, alphaviruses and polyoma viruses, see column 32, lines 26-67. Dubensky also teaches that the expression vector is a plasmid, see column 36, line 44 to column 37, line 16 and column 56, line 47 to column 57, line 11 for example. Dubensky teaches a cell containing the gene delivery vector in claim 12.

Dubensky also teaches that antisense RNA forming large quantities of double-stranded RNA is utilized in the expression system. The double-stranded RNA increases the expression of gamma interferon and boosts the expression of MHC I antigens, see column 23, lines 1-13. Dubensky also claims a vector construct expressing an antisense sequence or a non-coding sequence, see claim 10. The antisense sequence and the non-coding sequence recited in the claim encompass an antisense RNA that forms double-stranded RNA.

Therefore, Dubensky teaches a construct encoding a polymerase II promoter encoding an antigen from a pathogenic agent, as well as a construct encoding a nucleic acid that forms double-stranded RNA for the induction of interferon, see the previous citations.

Dubensky does not teach dsRNA with self-complementing sequences.

However, Gillespie teaches dsRNA with complementing sequences from a vector construct to induce the production of interferon. See page 4, line 10 to page 6, line 18, Figures 1-4 and claims 1-16.

One of ordinary skill in the art at the time the invention was made would have been motivated to express the complementing dsRNA of Gillespie in the vector of Dubensky to induce a therapeutically effective amount of interferon, see claims 9-16 of Gillespie in particular. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of expressing the dsRNA of Gillespie in the vector of Dubensky to induce interferon because both Dubensky and Gillespie express dsRNA from a vector to induce the production of interferon, see the previous citations of both references.

Dubensky does not teach a single construct expressing a heterologous antigen and another promoter encoding a nucleic acid that forms double-stranded RNA.

However, one of ordinary skill in the art at the time the invention was made would have been motivated to express a nucleic acid molecule that forms a complementary-stranded double-stranded RNA (as taught by Gillespie) and a viral antigen in the same construct to stimulate a specific immune response to the viral antigen, see column 37, line 35 to column 38, line 16, and to stimulate the production of

interferon, see column 23, lines 5-8 of Dubensky and claims 9-16 of Gillespie. In addition, Cella teach that double-stranded RNA induces interferon, protects against cytopathic effects of a virus in dendritic cells and increases the capacity of dendritic cells to prime T cells, see the abstract and the first two paragraphs in the discussion section on page 826. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to induce the production of interferon with the complementary, double-stranded RNA of Gillespie to protect dendritic cells from viral infection and generate a CTL response to a viral infection, see page 821 and the first two paragraphs in the discussion section on page 826 of Cella and elicit a specific immune response with the viral antigen of Dubensky.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing a construct expressing a heterologous antigen and another promoter expressing a double-stranded RNA because Dubensky teaches that the expression vector is used to express multiple heterologous genes, see column 16, line 61 to column 17, line 29 and column 85, line 50 to column 94, line 18. Therefore, the instant construct would have been prima facie obvious in view of the teachings of Dubensky, absent unexpected results to the contrary.

One of ordinary skill in the art at the time the invention was made would also have been motivated to express the heterologous genes of Dubensky from different promoters within the same construct because Chada teach that one promoter within the same construct may be inadequate to ensure an adequate level of expression of all heterologous genes, see column 26, lines 4-21.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in expressing different heterologous genes from different promoters in the same construct of Dubensky because the vector of Chada is also a eukaryotic layered vector initiation system, see column 14, lines 52-56. The eukaryotic layered vector initiation system of Chada utilizes the same viral vectors and the same promoters of Dubensky, see column 16, line 48 to column 17, line 21 of Chada. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Response to Arguments

Applicant points to page 22, lines 1-5 of the disclosure and Figures 1-3 to illustrate dsRNA via self-complementation and contrasts this type of dsRNA with the antisense RNA of Dubensky. Applicant argues that Cella does not teach expression cassettes and Chada does not teach dsRNA formed by self-complementation. Applicant further argues that Dubensky and Chada do not teach or suggest single expression cassettes that produce dsRNA that is self-complementary and that Cella is silent with respect expression constructs. Applicant concludes that there is a lack of motivation to combine the references and that no combination of references would lead the ordinary artisan to arrive at the instant subject matter claimed.

Applicant's arguments have been fully considered, but are found unpersuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA

1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). If any one of the references taught all of the limitations claimed, that single reference would have been applied against the instant claims as an anticipatory-type reference under a different statute. In the instant case, the limitations that are not taught in one reference are not only taught by another reference, but motivation to combine the teachings in the references with a reasonable expectation of success is also evident.

Dubensky teaches that expression of heterologous antigens stimulate a specific immune response to the antigen, see column 37, line 35 to column 38, line 16, and that double-stranded RNA stimulates the production of interferon, see column 23, lines 5-8. Dubensky also teaches expressing multiple heterologous inserts from a vector construct (see column 16, line 61 to column 17, line 29 as well as column 85, line 50 to column 94, line 18), whether or not these inserts express a gene or a non-gene.

Dubensky does not teach dsRNA with self-complementing sequences.

However, Gillespie teaches dsRNA with complementing sequences from a vector construct to induce the production of interferon. See page 4, line 10 to page 6, line 18, Figures 1-4 and claims 1-16.

One of ordinary skill in the art at the time the invention was made would have been motivated to express the complementing dsRNA of Gillespie in the vector of Dubensky to induce a therapeutically effective amount of interferon, see claims 9-16 of Gillespie in particular. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of expressing the dsRNA of Gillespie in the vector of Dubensky to induce interferon because both Dubensky and Gillespie express dsRNA from a vector to induce the production of interferon, see page 4, line 10 to page 6,

line 18 of Gillespie and claim 10 of Dubensky. The teachings of Cella provide further motivation for expressing dsRNA in the expression construct of Dubensky since double-stranded RNA induces interferon, protects against cytopathic effects of a virus in dendritic cells and increases the capacity of dendritic cells to prime T cells, see the abstract and the first two paragraphs in the discussion section on page 826 of Cella.

Dubensky does not teach expressing heterologous constructs from different promoters in the expression vector. However, Chada teaches that one promoter within the same construct may be inadequate to ensure an adequate level of expression of all heterologous genes, see column 26, lines 4-21. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in expressing different heterologous products from different promoters in the vector of Dubensky because the vector of Chada is also a eukaryotic layered vector initiation system, see column 14, lines 52-56.

In conclusion, the combination of references teach all of the limitations claimed and provide motivation for combining the teachings in the reference with a reasonable expectation of success, absent evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Patent Examiner, 1648